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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,464	08/06/2001	Konan Peck	08919-061001	1550

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EXAMINER	
QUAN, ELIZABETH S	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 04/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,464	PECK ET AL.	
	Examiner	Art Unit	
	Elizabeth Quan	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 05.12.2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 13-25 in the Response to Restriction Requirement mailed on 1/15/2004 is acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 18, 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is unknown what bubble point pressure is. What property of the membrane does the bubble point pressure measure or characterize?

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 13-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 13 is rendered indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The optimal dispersing pressure for a particular fluid is determined by measuring several coefficients of variation and

synthesis support scattering heights in the wells at different dispersing pressures for dispensing that particular fluid in order to find a balance between reagent accumulation at the nozzle tip and synthesis support spattering. The determination of the dispersing pressure is not based upon **a** coefficient of variation for each dispersed fluid as a function of the dispersing pressure and **a** synthesis support scattering height in the wells for each dispersed fluid as a function of the dispersing pressure. It appears that the specification uses "scattering" and "spattering" interchangeably and "dispersing pressure" and "ejection velocity" interchangeably which introduces some clarity issues. Although the last paragraph on page 2 of the specification uses the same language recited in clam 13, it does not provide an explanation of how the method is conducted. However, beginning on line 10 on page 6, there is a discussion of determining optimal ejection velocity by measuring coefficients of variation and spattering. If the claim is not directed to the explanation described in reference to fig. 6, then there is a 112, first paragraph issue.

7. Claim 14 is rendered indefinite since it is unclear what the gas flow rate and pumping rate is being referred to. Is it the gas flow rate by which liquids are being dispensed into the wells or the natural gas flow rate formed by suction of gas through the reaction medium? Is the pumping rate the rate at which the vacuum pump operates or the rate at which liquid drains from the wells? Additionally, it is unclear whether the wells are selected to have a synthesis reaction medium or the wells already have a synthesis reaction medium and is selected to have a gas flow rate less than a pumping rate. It is also unclear how selecting wells with reaction mediums figures into having a gas flow rate less than a pumping rate. It is unclear what the connection or cause and effect relationship is.

8. Claim 15 is rendered indefinite since it appears that the well is defined by a bore not the well defining a bore.

9. Claim 18 is rendered indefinite since the bubble point pressure of the membrane depends on the applied vacuum pressure, which has not been recited. In the instant specification, the applied vacuum pressure of 10 in. Hg yields a membrane bubble point pressure of 36.5-40.6 in. Hg.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 13, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,472,672 to Brennan.

Brennan discloses an apparatus and method for polymer synthesis using arrays (abstract).

Brennan discloses that there are two important concerns in liquid reagent delivery through nozzles: 1) how to eject a droplet cleanly so that a drop is not left hanging on the end of the nozzle, which corresponds to the coefficient of variation as disclosed in the instant specification; and 2) how to keep the contents of the reaction chamber from splashing when the stream of reagent is delivered into the well, which corresponds to the synthesis support s[p,c]attering height as disclosed in the instant specification (col. 7, lines 27-32).

Brennan further discloses that the ejection velocity must be sufficient to mix reagents delivered into a chamber (col. 7, lines 32-34). Very small droplets can be ejected cleanly at high

ejection velocities but do not have sufficient kinetic energy to overcome the surface tension of the liquid already in the well to cause mixing (col. 7, lines 34-38). Larger droplets eject cleanly at high velocities by tend to splash the contents into adjacent wells (col. 7, lines 38-40). At low ejection velocities, reagents leave the last drop hanging from the nozzle tip, which is also a function of the cross-sectional area of the tip (col. 7, lines 40-42). The flow rate of liquids through small capillary tubing varies directly with delivery pressure and inversely with each of the length and diameter of the tube (col. 7, lines 43-46).

Brennan emphasizes that all the above variables must be considered when developing delivery pressure and nozzle configuration and materials to cleanly expel reagents (col. 7, lines 46-50). Different reagents may have different optimal ejection velocities or delivery pressures (col. 7, lines 51-53). Since Brennan's invention takes into account all these factors, the development of the invention involved determining the optimal dispersing pressure by balancing the desire for clean droplet ejection and non-existence of splashing of the contents of the wells, which may include only the solid support on the membrane if the reagent has not yet been added. The latter criteria would require one to consider the spattering height, the height the solid support may reach at a certain dispersing pressure, since the solid support may spatter but still be retained in the well or spatter out of the well.

The optimal ejection velocity is used to dispense a plurality of reagents via the supply assembly (43) into a plurality of wells (26) of a parallel synthesis plate (25) (figs. 1-7; col. 5, line 39-col. 7, line 54). The supply assembly couples each bank of nozzles a common reagent reservoir (23) through independent dispensing tubes (44) (col. 7, lines 4-7). The distal end of each dispensing tube forms nozzles (22) (col. 17-26). The nozzles do not appear to have any

sharp edges, such that it is considered to have a de-burred tip. The delivery of reagents through the nozzles (22) is controlled by an array of independent valve assemblies (55) each mounted in-line therewith (col. 7, lines 59-61). The valve assemblies are preferably provided by solenoid driven micro shutoff valves (col. 7, lines 61-65). The dispensing tubes, which forms the nozzles, is made from TEFLON, which is the preferred material having a surface energy of about 20 dynes/cm or less as disclosed in the instant specification (col. 7, lines 4-20). It appears that the supply assembly is configured to provide fluids to wells in volumes as small as about 2 microliters since the valves are capable of opening and closing in less than 5 milliseconds to deliver reagent. Each well is defined by a bore extending from a first end to a second end (figs. 1-7). A retaining device (84) is positioned in the bottom of each well between orifice (74) through which the contents of each well is drained and solid support (75) (col. 10, lines 55-66). The retaining device is preferably provided by a polyethylene or glass fiber frit, which acts as a filter membrane permitting reagent solution to flow therethrough while retaining the solid support and polymer chain grown thereon in the well (col. 10, lines 59-66). The retaining device is made from filter frit membranes, which is the preferred material for obtaining bubble point pressures above the applied vacuum pressure of 10 in. Hg as disclosed in the instant specification. The solid support is controlled pore glass (CPG) (col. 2, lines 4-21; col. 12, lines 14-37; col. 13, line 14-col. 16, line 47).

Draining of the reactions wells is effected by creating a pressure differential exceeding a predetermined amount (col. 10, line 9-col. 12, line 1). Increasing the pressure differential to about 5 psi effects rapid purging of the wells (col. 10, line 9-col. 12, line 1). Generally, it is necessary to maintain a pressure differential between about 2.5 psi to about 5 psi to sufficiently

drain the reaction wells simultaneously of reagent solution (col. 10, line 9-col. 12, line 1). As the wells begin to empty, the flow rate of inert gas through the empty wells substantially increases, which decreases the pressure in common chamber (31) (col. 10, line 9-col. 12, line 1). This decrease in interior pressure further decreases the draining rate of the reagent solution the orifice, an effect magnified by retaining filter membrane (84) (col. 10, line 9-col. 12, line 1). The pressure differential may be created by forming a vacuum in lower catch basin (81), which is located at the second end of the wells, by coupling the basin's drain outlet (83) to a vacuum pump (col. 10, line 9-col. 12, line 1). The pressure differential may be created from a combination of positive pressure in common chamber (31) and vacuum in catch basin (81) (col. 10, line 9-col. 12, line 1).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 15-19, 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,472,672 to Brennan in view of U.S. Patent No. 6,171,780 to Pham et al.

Brennan discloses that the synthesis apparatus is configured to employ a 96-well microtiter plate, aligned in 12 equally spaced apart rows by 8 equally spaced apart columns (col. 6, lines 10-17). Brennan further discloses that any number or wells or arrangement of rows and columns could be employed without departing from the true spirit and nature of the invention (col. 6, lines 19-23). Brennan does not address the diameter or spacing of the wells or explicitly disclose using more than 1000 wells in performing synthesis. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the microtiter plate of Brennan to provide at least 1000 wells each with an inner diameter of less than about 3.0 mm spaced center-to-center by about less than 4.5 mm since it is very well known to use different microtiter plates for different needs, such as a microtiter plate with more than 1000 wells to perform at least 1000 assays simultaneously with limited amounts of sample, as taught by Pham et al. (col. 11, line 44-col. 13, line 10). Additionally, in the event one would argue that the supply assembly is not configured to provide fluids as small as about 2 microliters,

it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Brennan to reconfigure the supply assembly by reducing the diameter of the nozzle or the size of the entire assembly or the length of time the valve opens and closes since it is very well known and useful to dispense microliter or nanoliter quantities in the effort of performing more assays more quickly without wasting samples and reagents.

16. Claims 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,472,672 to Brennan.

Brennan discloses conducting a 20 nanomole scale reaction (col. 15, lines 42 and 43). Brennan does not explicitly disclose conducting less than 20, 10, or 5 nanomole scale reactions. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Brennan to conduct even smaller scale reactions, such as 5 nanomole scale reactions, in the effort of high throughput by saving time from dispensing less reagents and samples, waste reduction, and as necessary or desired to perform an experiment.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Quan whose telephone number is (571) 272-1261. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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